REMARKS

Claims 1-18 are pending. Claims 1-14 have been withdrawn, and claims 15-18 are currently under examination on the merits. Claims 15, 16, and 18 have been amended herein. Applicants respectfully submit that the claim amendments are fully supported in the specification as filed, and do not introduce new matter.

The Claims are Sufficiently Definite

Claims 15-18 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The recitation "flexible elastically deformable" in clam 15 is allegedly indefinite in its failure to specify a temperature at which the material is deformable. Applicants have amended the claim which now recites a "flexible material that is elastically deformable at room temperature." Accordingly, the rejection is moot. Reconsideration and withdrawal of the rejection of claims 15-18 with respect to this recitation is respectfully requested.

Claim 16 also stands rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite in its recitation of "the receptacle of the at least one suspension specimen into which at least one specimen chamber is inserted" as it was allegedly not clear what was being inserted into what. The claim has been clarified by amending to establish that "at least one suspension specimen is inserted into a corresponding specimen chamber." Accordingly, the rejection is moot. Applicants respectfully request reconsideration and withdrawal of the rejection of claim 16 under 35 U.S.C. § 112, second paragraph with respect to this recitation.

Claim 16 stands further rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite in its recitation of "the receptacle" which allegedly lacks proper antecedent basis. The allegedly offending recitation has been deleted, obviating the rejection. Applicants respectfully request reconsideration and withdrawal of the rejection of claim 16 under 35 U.S.C. § 112, second paragraph with respect to the recitation of "the receptacle."

Claim 18 stands rejected in its recitation of adjacent to "the frame elements of the carrier", which is allegedly unclear and subject to multiple interpretations. The recitation in claim 18 has been amended to recite "frame parts of the carrier", which in view of the amendments to claim 15 and 16 are sufficiently definite within the meaning of 35 U.S.C. § 112, second paragraph. The Examiner is respectfully requested to consider Figure 9, and the disclosure on pages 13-14 relating to removal of chamber sections. The skilled artisan would

readily be able to apprehend what is being claimed by the Applicants. Accordingly, reconsideration is requested, followed by withdrawal of the rejection.

In view of the clarifying amendments made herein, all of the claims are sufficiently definite. Reconsideration consistent with the foregoing is requested, and appropriate.

The Claims Are Patentable Over the Cited References

Claims 15-1 8 stand rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Studer (U.S. Patent Application Publication 2002/10108957).

The Office Action alleges that claim 15 recites a method for storage of at least one suspension specimen in a low-temperature state, comprising the steps of: accommodating the at least one suspension specimen in at least one specimen chamber made of a flexible elastically deformable material; mounting the specimen chamber in a carrier according to claim 1 (which recites a carrier for at least one specimen chamber. comprising a mounting frame for positioning the specimen chamber, wherein the mounting frame has a first frame part and a second frame part which can be joined together detachably using connecting elements and which come in contact on side faces of the frame parts in the assembled state, wherein the specimen chamber can be secured between the side faces of the mounting frame. so that the specimen chamber is immovable relative to the mounting frame), wherein the specimen chamber is secured between the frame parts; and converting the suspension specimen to a low-temperature state by positioning the carrier with the specimen chamber in a cryomedium. Claim 16 allegedly recites the method above, wherein the receptacle of the at least one suspension specimen into which at least one specimen chamber is inserted by immersing the at least one specimen chamber with one inlet end into a specimen reservoir and transferring the suspension specimen under the influence of a vacuum applied to the corresponding outlet end or under the influence of capillary forces. Claim 17 allegedly recites the method of claim 15, wherein at least one partial specimen is detached from the at least one specimen chamber in the low-temperature state by mechanical separation. Claim 18 allegedly recites the method of claim 17, wherein the mechanical separation comprises cutting off chamber sections of the specimen chamber adjacent to the frame elements of the carrier.

The Office Action alleges that Studer teaches a method for the storage of at least one suspension specimen (i.e. hydrous specimen) in a low-temperature state by accommodating the suspension specimen in at least one specimen chamber, which may be of a flexible material (a porous polymer; abstract, p. 4, par. 41). The Office Action further states that Studer teaches mounting the specimen chamber with the specimen in a carrier, wherein the specimen chamber is secured between the frame parts (pp. 4-5, par. 48-49, figs. 4A and 4B). The carrier taught by Studer (see fig. 4A) allegedly comprises a mounting frame for positioning the specimen chamber (1 7) with a first and a second frame part (1 3) that can be joined together detachably using connecting elements (17) and that come into contact with side faces of the frame parts in the assembled state (17): wherein the specimen chamber can be secured between the side faces of the mounting frame so that it is immovable relative to the mounting frame (pp. 4-51 par. 48-49, fig. 4A). Studer also allegedly teaches that the suspension specimen is converted to a low temperature state by positioning the specimen in a cryomedium (p. 5; par. 50). According to the Office Action, Studer teaches that the specimen is transferred into the specimen chamber by suction or under the influence of vacuum forces (p. 4, par. 46).

Studer also allegedly teaches that a partial specimen may be detached from the specimen chamber in the low temperature state by mechanical separation, such as by cutting off chamber sections (p. 4, par. 41. p. 5, par. 52).

The Office Action acknowledges that although Studer teaches that the first and second frame parts come into contact with the side faces of the frame parts in the assembled state, Studer does not teach that first and second frame parts come into contact with each other on side faces of the frame parts in the assembled state. However, the Office Action asserts that it would have been a matter of routine experimentation to develop an apparatus wherein at least one of the first or second frame parts (i.e. 13 in fig. 4A) was connected to the mounting frame (i.e. 17 in fig. 4A), resulting in an apparatus for practicing the method wherein the first and second frame parts come into direct contact with each other. The Office Action further acknowledges that Studer also does not teach that the suspension specimen is converted to a low temperature state by positioning the specimen in a cryomedium with the carrier, however it alleges that Studer does teach that the suspension specimen is exposed to the cryomedium within the carrier. The Office Action asserts that inserting the carrier and the specimen

within the cryomedium to further facilitate cooling of the specimen would also have been a matter of routine experimentation. Additionally, Studer teaches that the cutting of the specimen in the specimen chamber occurs after the specimen chamber is removed from the carrier, and not that the cutting of the specimen occurs adjacent to the frame element of the carrier. According to the Office Action, a skilled artisan would have recognized that the cutting step could have been performed at any stage during the procedure, and would have been motivated to alter the procedure by cutting the specimen earlier in the process because Studer teaches the desirability of immediate removal and processing of the samples after freezing (p. 5, par. 51-52). One of ordinary skill in the art would allegedly have had a reasonable expectation of success in performing the claimed procedure because methods for crypreservation of hydrous samples were well known in the art at the time of the invention, as taught by Studer (p. I, col. I). The Office Action concludes that it would therefore have been obvious to one of ordinary skill in the art to modify the teachings discussed above to develop the claimed invention. Thus, the claimed invention, as a whole, was allegedly *prima facie* obvious over the combined teachings of the prior art.

Applicants respectfully traverse the rejection. Contrary to the assertions in the Office Action, the skilled artisan would not have arrived at the claimed invention through mere application of routine experimentation to the teachings of Studer. Second, there would have been no motivation or rational basis at the time, to modify Studer in the proposed manner because the specimen holder of Studer is not at all related to the carrier of the claims and could not function as such. Assuming, *arguendo*, that the asserted Studer references was so modified, there could not have been a reasonable expectation of success. Further, the proposed modifications are impermissible under the MPEP. Finally, the references teach away from the proposed combination.

Applicants respectfully submit that Studer does not teach the method as claimed, and that the design of Studer's specimen holder device precludes the practice of the methods now claimed even with the allegedly routine experimentation proposed in the Office Action. Studer is directed to an entirely different type of cryopreservation apparatus and methods used therewith. In particular, Studer discloses various specimen holders for use in high-pressure cryopreservation systems. Studer's invention does not relate to the carrier of the

claims. The carrier of the claims is stored in the low temperature state with the suspension specimen. Studer teaches specimen *holders* for receiving a hydrous sample in a specimen chamber (Studer's capillaries, e.g. cellulose). While the capillaries are deformable, the specimen holder is adapted solely for use in the high-pressure freezing apparatuses Studer teaches. Studer's specimen holders are an integral part of the high pressure freezing circuit and the carriers and specimen chambers of the instant claims are not compatible with Studer's high-pressure freezing circuit, and vice versa. Thus modifying Studer's method would not result in the claimed method because they are simply entirely different apparatus for entirely different purposes. One proposed modification would entail opening the high pressure freezing circuit to remove the sample "earlier in the process," but would require at least partially thawing the sample to do so. It simply would *not* be possible to modify Studer in the proposed manner to arrive at the claimed invention, and assuming *arguendo* that it is possible, it certainly would not be routine to modify a high-pressure freezing apparatus to perform the claimed method. Cutting of the specimen from the Studer device also would not readily be accomplished adjacent to the frame because the capillary containing the specimen is essentially frozen to the specimen holder by way of the hydrocarbon layer which must also be melted/thawed before the sample can be removed from the holder. Finally, it would not be feasible or reasonable to *store* the carrier of Studer in the low-temperature state with the specimen, as the Applicants' claim requires.

Additionally, Studer does not permit direct contact between the mounting frame and the specimen chamber. They are always separated by a layer of fluid, e.g. hydrocarbon. Further, the inclusion of this layer requires the use of partial "thawing", e.g. in the cryostat to remove the capillary with the specimen from the specimen holder upon melting of the interceding layer. Applicants' claim 15 provides "connecting the first and second frame parts into an assembled state **wherein the first and second frame parts come into *contact* on side faces of the frame parts *and with the specimen chamber***, such that the specimen chamber is immovable relative to the mounting frame."

Applicants further submit that there would have been no motivation whatsoever to make the modifications proposed by Examiner regarding inserting the carrier of Studer as well as the specimen within the cryomedium to facilitate further cooling. Studer's apparatus is designed as an integral part of a high-pressure freezing circuit as shown in his Figure 4A.

It is completely contrary to its design and principle of operation to insert both Studer's "carrier" and specimen chamber into the cryomedium to effect the freezing of the sample. (see below). At the time of initial freezing, the specimen holder must be physically in the circuit with the pressure-generating piston (24). This reinforces the fact that Studer does not teach a "carrier" as is claimed by Applicants, but rather a "specimen holder" for use in a high-pressure freezing system. Thus, Studer's specimen chamber is placed in the cryomedium, e.g. liquid nitrogen, only *after* the specimen has been initially frozen and removed.

There also would be no motivation to make the proposed modifications suggested in the Office Action. There is no need or motivation to bring the first and second frame parts (13) of Studer into contact with each other. No benefit would accrue to the skilled artisan. As can be seen, the sample is placed between them, and there would not be any advantage to moving them closer to each other, or into contact with each other. Such positioning would interfere with the amount of space in the cavity (16) (see Figure 4 of Studer) and quite likely that would interfere with the cooling of the specimen. See e.g. Studer at page 4, paragraph [0048], last sentence stating "[t]his [cavity] is necessary in order to allow the greatest possible volumes of the coolant (K) per unit of time to impinge on the specimen holder. Thus Studer himself *plainly teaches away* from the proposed modification because the space that defines the cavity is necessary in Studer's words. Such a teaching away would preclude moving the frame parts closer.

In addition because the proposed modification would completely change the principle of operation, such modification is precluded as a basis for a finding of obviousness. The proposed modification cannot change the principle of operation of the reference (here, Studer), as this would contravene MPEP 2143.01 Part VI. As the MPEP discusses, in *In re Ratti,* the Federal Circuit's predecessor court held that

> [The] suggested combination of references would require a substantial reconstruction and redesign of the elements shown in [the primary reference] as well as a change in the basic principle under which the [primary reference] construction was designed to operate.
> *In re Ratti*, 270 F.2d 810, 813, 123 USPQ 349, 352 (CCPA 1959)

The asserted modification of Studer here would require extensive changes and substantial reconstruction of Studer's specimen holder and high-pressure freezing apparatus.

There is no suggestion for making those changes in the references themselves, or in the art. The proposed changes include closing or reducing the cavity which Studer teaches is **necessary**, and opening the high-pressure circuit at an "earlier point" in the process to facilitate cutting, and placing the carrier and the specimen into the cryomedium, whereas Studer's actual system does not involve any such step because the sample is first frozen in the specimen carrier, then later removed and placed in a cryomedium for storage.

Finally, Studer is not suited for handling more than one specimen, whereas the claim is directed to at least one suspension specimen. For example, the Applicants' claimed method is well-suited to (but not limited to) a plurality of specimen chambers in a single mounting frame or specimen holder, whereas that is clearly beyond the scope of Studer.

In view of the foregoing, reconsideration is respectfully requested. Withdrawal of the rejection under 35 U.S.C. § 103 (a) in view of Studer is also requested.

Conclusion

This response is believed to fully responsive to the issued Office Action. The claims are in condition for allowance. An early and favorable action to that end is earnestly solicited. The Examiner is invited to contact Applicants' undersigned representative to resolve any outstanding issues prior to allowance.

Respectfully submitted,

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